Environmental Health

The year 2000 is fast approaching and bringing with it a host of challenges and opportunities for the protection of environmental health. Environmental health stakeholders in the government, industry, and public interest sectors are looking back on past achievements and failures and setting priorities for the future. The environmental health stakes may be higher now than ever before. With the dawning of a new millennium, a historical threshold is being crossed—localized pollution problems of the past are giving way to what may be irreversible environmental changes affecting both the global ecosystem and global economics.

Due to substantial differences in population growth rates and levels of economic development, environmental health priorities for the year 2000 will differ sharply between the developed and developing worlds. Many developed nations are building on years of well-funded environmental programs that have done much to increase sanitation, reduce levels of environmental pollution, and improve public health. Priorities in these countries will focus largely on remaining problems such as minimizing chronic low-level exposures to pesticides and other chemicals, and continuing to study and assess their toxicological effects.

Environmental health priorities of the developing world, on the other hand, will reflect the often overwhelming pressures of population growth and rapid industrialization. Many developing countries are decades behind the developed world with respect to environmental protection. These countries continue to face poor sanitation and related increases in diseases such as malaria, diarrhea, and cholera. Critical shortages of safe drinking water are a serious problem, as are exposures to highly polluted air, industrial chemicals, and agricultural pesticides—problems that will be solved only through a coordinated, international effort. Among the most challenging environmental priorities of the 21st century, global climate change is one that will be shared by developed and developing nations alike.

Is It Toxic?

One of the most pressing environmental health priorities for the developed world in the 21st century is posed by the thousands of industrial chemicals for which even the most basic test data are not available. According to the EPA report *Chemical Hazard Data Availability Study*, released in April 1998, only 7% of the 3,000 high production volume chemicals (HPVs) currently used in commerce in the United States have a comprehensive set of basic health and environmental effects studies available to the public. The EPA defines HPVs as substances for which imports or production quantities exceed 1 million pounds per year. "How can you have meaningful sustainability approaches if you don't know what's toxic and what isn't?" asks Karen Florini, a senior attorney with the Environmental Defense Fund (EDF), based in New York City. "You need data using validated approaches."

Conducting screening-level toxicity tests on these uncharacterized chemicals was

identified as a top priority for the year 2000 by a number of influential United States stakeholder organizations, including the EPA, the EDF, and the Chemical Manufacturers Association (CMA). "We agree with the EDF that there is a need to fully characterize the HPV chemicals, and this will be a major focus for us over the next several years," says Mort Mullins, vice president for product stewardship and research at the CMA.

The procedural mechanism that these groups will use to guide their research is the Screening Information Data Set (SIDS) program, which was developed in 1990 by the Paris-based Organisation for Economic Cooperation and Development (OECD), an intergovernmental organization focused primarily on setting economic and environmental policy. The OECD developed the SIDS program as a systematic means by which member countries could cooperatively review the safety of the roughly 85,000 chemicals used in international commerce. HPVs top the list, under the assumption that production volume is perhaps the best indicator of potential exposure. Data categories covered under the SIDS program include physical and chemical properties, environmental fate and transport, ecotoxicological effects, and mammalian toxicity. However, the data requirements within each of the categories are minimal. The overriding intent of the program is to classify chemicals according to potential hazard, and flag those that may require additional testing. In this respect, the SIDS data are insufficient for use in quantitative risk assessments, which rely on bioassays for extrapolating toxicity at a range of doses in multiple species.

The representative to SIDS from the United States is the EPA Office of Pollution Prevention and Toxics. In response to a major expansion of the Chemical Right-to-Know (ChemRTK) Initiative, unveiled by U.S. Vice President Al Gore in April 1998, the EPA established the HPV Challenge Program, which prescribes an aggressive research program directed at gathering baseline data on uncharacterized industrial chemicals. According to the EPA, providing the public with a complete SIDS dossier for all HPVs would cost the chemical industry a total of approximately $427 million, roughly 0.2% of the total annual sales of the top 100 U.S. chemical companies. Says Lynn Goldman, assistant administrator of the EPA Office of Prevention, Pesticides, and Toxic Substances, "Right now we have a trickle of information available on HPVs. We're hoping to turn that trickle into a [flood]. There's going to be a very concerted effort to have all of the SIDS data gaps filled as soon as possible."

Chemical Right to Know

In keeping with an expansion of the ChemRTK Initiative, which was cited as a primary EPA agenda item for the future in the September 1997 report *EPA Strategic Plan,* Goldman adds that both the EPA and the CMA, as well as a number of other industry and environmental groups, are currently holding discussions on the most effective ways to disseminate SIDS and other related chemical toxicity information to the public. Certainly a key tool that will be increasingly used to facilitate the flow of this kind of information will be the Internet. Another influential group using the Internet to promote right-to-know initiatives is the EDF. According to Florini, expanding right-to-know initiatives is a major year 2000 agenda item with the organization, which will especially focus on continuing to develop the Chemical Scorecard, an EDF-sponsored Web site that provides toxicity information to the public via a series of links to over 150 separate databases. As one of its most intriguing features, people can access information on chemical releases in their own communities simply by typing in their ZIP codes. "This is a pilot effort designed to make aggressive use of currently available information and provide it to both the public and companies that produce or use chemicals in a user-friendly fashion," Florini says, adding, "[The site has] already gotten over 10 million hits."

The almost instantaneous posting of toxicity information on the Internet as it becomes available is somewhat disconcerting to the industry, however, which is increasingly looking to promote risk- rather than hazard-based decision making in environmental policy. Roger McClellan, president of the Chemical Industry Institute of Toxicology (CIIT), an industry-funded toxicology research facility based in Research Triangle Park, North Carolina, is concerned that rapid dissemination of hazard-based information—such as SIDS data—may alarm the public unnecessarily. "We're at a crossroads now with respect to achieving the goal of control and minimization of human health risk from the use of chemicals," he says. "Hazard-based systems are closely aligned with fear. Using screening-level tests, chemicals may be identified as potentially hazardous, but you're left without information that supports levels of safe versus nonsafe exposure. One is left with the impression that there is no safe exposure."

Speeding up Toxicity Assessment

Unfortunately, even screening-level testing, let alone more involved mechanistic assessments and potency evaluations, is seriously constrained by the elements of time and money. Conservative estimates suggest that, at its current pace, testing the remainder of the HPVs on the SIDS target list could take as long as 25–30 years. A number of environmental officials and industry representatives are therefore calling for improved efficiency of toxicity testing as a priority agenda item for the future. Of particular interest in this regard are "high throughput technologies," which are *in vitro* techniques initially developed by the pharmaceutical industry to quickly assess efficacy and potentially adverse reactions in new products. "Some of the technologies coming down the line are just mind-boggling," says McClellan. "These techniques can be used to screen thousands of chemicals using automated systems. This is a powerful tool." Kenneth Olden, director of the NIEHS and the National Toxicology Program, agrees. "One of our biggest priorities is to develop high throughput techniques to test for carcinogenicity [and other toxic effects]," he says. The NIEHS will continue to develop transgenic animal models and sophisticated *in vitro* testing procedures that Olden says could reduce the time required for carcinogenicity evaluations from 2 years to 3–6 months, and that use fewer animals.

In developing additional procedures that can be used for carcinogenicity and other evaluations, the NIEHS will be relying in part on the recommendations of the Interagency Coordinating Committee on the Validation of Alternative Methods, an ad hoc organization composed of representatives from 14 federal scientific and regulatory agencies. The committee was convened

Only 7% of the 3,000 high production volume chemicals currently used in commerce in the United States have a comprehensive set of basic health and environmental effects studies available to the public.

by the NIEHS in 1994 to establish criteria for the validation of alternatives to standard toxicological testing protocols. The committee was formed in response to a congressionally mandated directive to reduce the use of animals in toxicity testing, a goal that is becoming increasingly popular with the public.

Continued Focus on Sensitive Populations

A chemical's innate toxicity is only part of the picture, however. Just who is exposed to environmental pollutants is also a critical factor, and an emphasis on sensitive subpopulations—particularly children—is steadily gaining momentum within the government, industry, and public interest sectors. Almost every major environmental and health organization has cited children's sensitivity to chemicals as a major research and advocacy priority for the year 2000.

The focus on children's health in the United States comes amidst a backdrop of mysterious increases in incidence rates for a number of childhood diseases, particularly childhood leukemia, pediatric brain tumors, and asthma. Children's health issues drove passage of the 1996 Food Quality Protection Act, which mandated that 9,000 current pesticide tolerances be reevaluated within the next 10 years to determine whether they are sufficiently protective of children.

According to Olden, the NIEHS is currently establishing a group of eight multidisciplinary children's environmental health centers through cooperative partnerships with the EPA and the Centers for Disease Control and Prevention. Olden outlines a number of research priorities at the NIEHS relating to children's health that will continue in the year 2000, including investigation of the effects of metals on intellectual development, asthma prevention strategies in inner cities, studies on the effects of air pollution, and studies on the developmental effects of pesticides. A complementary agenda is in place at the EPA, which is concentrating on identifying risk parameters that differentiate children from adults, investigating the highest priority environmental threats to children, and developing programs looking at environmental causes of childhood asthma. Under the ChemRTK Initiative, the EPA is also establishing a Children's Test Rule under the Toxic Substances Control Act, in which chemicals that may pose a particular risk to children will be extensively evaluated. According to Mullins, approximately 100 chemicals have been tentatively selected for review thus far. However, the list won't be finalized until December 1999, pending further input from the Children's Health Protection Advisory Committee, which is chaired in part by representatives of several CMA member companies, in addition to EPA officials and environmental activists. Environmental groups are also heavily vested in children's environmental health. For example, the Natural Resources Defense Council (NRDC) is participating on the Children's Health Protection Advisory Committee and has made implementation of the Food Quality Protection Act one of its major agenda items. According to Gina Solomon, a physician and senior scientist with the organization, the NRDC plans to devote a large portion of its environmental health budget to this issue in the years to come.

Children are but one sensitive subpopulation on the priority list for the year 2000, however. Says Olden, "It's clear that not everybody is identical in terms of response. Age is one reason, but genetics, poverty, and nutritional status also account for differences in susceptibility." The NIEHS's Environmental Genome Project, which is paving the way toward identifying genetic factors that contribute to susceptibility, will continue to receive major funding in the year 2000. This effort is attempting to identify DNA variants for environmental susceptibility, as well as to promote population-based studies of gene–environment interactions in the development of disease. Over 200 specific genes currently suspected to be involved in the development of environmentally related illnesses are slated to be studied. According to Olden, identifying individuals that are at increased risk because of their genetic makeup will go a long way towards achieving the goal of regulating chemicals to protect the most sensitive populations. "It's going to have a big impact on public health," he says.

Industry is also committed to applied research in the area of genetic susceptibility to chemicals. The CIIT, for example, recently identified *in vivo* the primary isozyme responsible for metabolizing benzene to its carcinogenic metabolite, using a transgenic mouse. According to McClellan, the CIIT will continue to perform studies such as these using transgenic animals to mimic sensitive human populations. McClellan says this work complements the work of the Environmental Genome Project and may prove useful in identifying human populations at enhanced genetic risk from exposure to environmental carcinogens.

Chronic Toxicity End Points

Additional year 2000 priorities in environmental health research are directed towards investigating subtle effects resulting from chronic low-level chemical exposures. "It's becoming clear that there's a new paradigm in toxicology," says Solomon. "There's a lot of emphasis now on subtle effects, especially endocrine, neurobehavioral, and immune effects. [With respect to neurobehavioral effects], we're seeing epidemics of attention deficit disorder, hyperactivity, and learning disabilities in children," she says, adding that "there is some evidence to suggest a link to chemical exposures. The NRDC is investigating this issue area. The policy implications are possibly huge. If we have these subtle effects at low doses, how will we determine acceptable exposure levels?"

In the last several years, highly publicized concerns have been raised that endocrine disruption caused by a variety of naturally occurring and synthetic chemicals could be linked to hormonally sensitive cancers, decreased sperm counts, and developmental defects in the male reproductive tract of both humans and wildlife species. Endocrine-mediated effects will continue to be a priority for the EPA, the CIIT, the CMA, and the NIEHS, all of which are involved in collaborative efforts to elucidate mechanisms and develop effective testing procedures for chemicals. The EPA recently announced its intention to screen 15,000 chemicals for endocrine-disrupting effects using high throughput technologies. This plan comes in response to the recommendation of the Endocrine Screening and Testing Advisory Committee, an independent advisory group of government, industry, and academic scientists convened by the EPA in 1996. According to McClellan, the CIIT is looking specifically at extrapolating reproductive effects in whole mammals from the results of molecular *in vitro* studies of chemicals on the estrogen receptor. Additional efforts will focus on chemical interactions with the androgen receptor, as well as additional effects not mediated by steroid receptors.

Exposure Assessment

Exposure assessment, often considered the weakest link in risk assessment, will also be an environmental health research priority in the year 2000 and beyond. According to Linda Sheldon, the lead scientist for human exposure measurement studies at the EPA National Health and Environmental Effects Research Laboratory in Research Triangle Park, a critical motivator for much of this research is changes in environmental legislation, such as the requirement for improved estimates of childhood exposures to pesticides under the Food Quality Protection Act. "We are looking at all the ways that children can be exposed to pesticides in their homes, and developing data

and models that can be used to predict those exposures," Sheldon says. Solomon says the NRDC will focus on addressing pathways of exposure that have been overlooked in the past, such as ingestion exposures via hand-to-mouth activities in young children and evaluating the use of biomonitoring data to estimate total exposures.

Another area of continued exposure research in the next decade will be the use of biomarkers—trace residues or chemical metabolites that can be used to identify and measure concentrations of a chemical in the body. Perhaps the most intensive effort in this regard is the NIEHS's Body Burden 2000 project, an ongoing interagency effort directed at measuring levels of several major pollutants in blood and urine. "We need to determine exactly what people are exposed to, and we need direct measures to do this," says Olden. "Measuring contaminants in environmental media doesn't describe the internal dose. We are going to develop large-scale population-based studies so we can begin to make policy decisions based on real information."

The Body Burden 2000 project will build on pilot studies conducted with the Centers for Disease Control and Prevention that are currently in their second year. These studies are measuring blood and urine concentrations of environmental estrogens, including dieldrin, mirex, DDT, polychlorinated biphenyls, and dioxins, among others. According to Olden, future studies will expand on this list of chemicals. A major goal of the project is to use chemical body burden information to identify populations that are at greatest risk, and to design appropriate intervention strategies to minimize their exposure.

Priorities in the Developing World

According to the World Resource Institute's (WRI) 1998 report *1998–99 World Resources: A Guide to the Global Environment*, environmental conditions in the developing world are a significant source of ill health for much of the population. In the least developed countries, as many as 20% of all children die before their fifth birthday. Horst Otterstetter, director of the Division of Health and Environment with the Pan American Health Organization (PAHO), says that much of the morbidity in developing countries results directly from exposure to contaminated water supplies. According to the WRI report, as many as 1.4 billion people worldwide don't have access to safe drinking water, and local populations often resort to collecting precipitation using open storage tanks and roof drains. Without treatment, this water can become contaminated with a variety of diarrhea-causing pathogens such as *Escherichia coli*. Diarrhea is one of the biggest killers in the developing world; it afflicts 4 billion people annually worldwide, and 2.5 million people died from it in 1996 alone.

Given the gravity of the problem, Otterstetter says that as much as 70% of PAHO's resources for environmental health in the year 2000 will be dedicated to safe drinking water programs in the poorest regions of Latin America. "Compared to drinking water, all our programs have to take a step back," he says. Expanding treatment of water systems with chlorine is a major goal of the organization, although Otterstetter comments that cultural conflicts can sometimes complicate these efforts. For a variety of reasons, community members are sometimes suspicious of such treatment and will occasionally refuse it.

"Underdeveloped countries are faced with double jeopardy," says Devra Davis, program director for health and environment at the WRI. "In addition to the traditional problems of dirty air and water, they also have to deal with the emerging problems of rapid industrialization." In countries such as Thailand, for example, the pace of industrialization has overwhelmed efforts to keep up with industrial emissions and chemical waste disposal. According to Otterstetter, PAHO will focus its efforts in the area of chemical contamination on reducing atmospheric pollutants in urban air, reducing exposures to heavy metals such as lead, arsenic, and mercury, and conducting education programs on the proper handling of pesticides and solvents. Says Otterstetter, "Overuse of pesticides is standard in Latin America. People figure that if a little bit will work well, a lot must work better."

Global Climate Change

The environmental priorities of both the developed and developing nations will converge substantially in the area of global climate change, which has the potential to affect human health worldwide. In many ways, this single issue, with its specter of rising sea levels, dramatic changes in weather patterns, oppressive heat waves, and the spread of tropical diseases to temperate climates, has the potential to dwarf other items on the international environmental agenda. An important environmental priority for the year 2000 will therefore be to continue looking for ways to implement the goals of the 1997 Kyoto Protocol, under which developed nations are seeking to reduce their emissions of greenhouse gases to levels approximately 5% lower than 1990 levels by the year 2012. "Certainly the largest global issue is climate change and greenhouse gas emissions," says Goldman. "We have to carry out the principles of the Kyoto conference and continue looking for reductions in greenhouse gases." However, the extent to which developing nations will participate in reducing greenhouse gas emissions remains to be seen. The Kyoto Protocol did not bind developing nations to any specific emissions limitations. Rather, it established a "clean development mechanism," which allows developed countries to receive pollution reduction credits by investing in projects in the developing world that reduce greenhouse gas emissions. However, this option has won only limited favor so far among developed countries, and the uncertain nature of any meaningful participation in the treaty by developing nations still has the potential to derail its goals.

As many as 1.4 billion people worldwide don't have access to safe drinking water.

In the long run, social, economic, and environmental sustainability will depend largely upon effective prioritizing among policy makers and on the success of the programs they implement. A continuing question will be how to balance environmental priorities as they compete for increasingly limited resources. But the consequences of failing to act have become clear; to relegate environmental concerns to the back burner of domestic and international policy is to impose upon yet another generation an unacceptable burden of avoidable health risk. As the world's population continues to grow, environmental problems are multiplying exponentially. It is possible that successful control of these problems in the next hundred years will predict continued success of the human race for the next thousand.

Charles W. Schmidt